

WILLARD J. STONE, M. D. (65 North Madison Avenue, Pasadena).—Every physician who has witnessed the sudden and, in many instances, unexpected death of a patient from pulmonary embolism during convalescence from a surgical operation, will appreciate Doctor Breyer's thoughtful review of the methods which may be used to prevent such a tragic accident.

From the medical standpoint, the circulatory condition of obese patients with slow heart rates and subnormal metabolism may be improved by the administration of thyroid extract during the first ten days of convalescence. Likewise the administration of glycocholl, for its general stimulating action on metabolism, leading to improved circulatory efficiency, may be helpful. The routine use of digitalis during convalescence whenever the heart rate is increased as a result of surgical shock, is difficult to justify from a pharmacologic standpoint. Its use should be limited, as Doctor Breyer has emphasized, to the treatment of auricular brillation and cardiac decompensation. With other forms of cardiac insufficiency, especially if the heart rate is slowed, the administration of theobromin or theophyllin salts may be beneficial. Strychnin as a circulatory tonic has gradually become less popular because of the insufficient dosage commonly employed. For patients with slow heart rates who may be believed to be unusually susceptible to thrombotic tendencies, the dosage should approximate one-tenth grain four times daily.



H. BRODIE STEPHENS, M. D. (384 Post Street, San Francisco).—Doctor Breyer has presented an excellent review of the distressing complication of postoperative thrombosis and embolism. The author in his review rightly emphasizes the frequency of this complication and, because of its frequency, a discussion of the subject is timely.

A careful study and adherence to the principles laid down by Doctor Breyer will undoubtedly frequently prevent this complication; or, if thrombosis does occur, its seriousness will be lessened by adopting the general principles set up by the author.

Notwithstanding the thoroughness of this paper, all will agree, I believe, that there will be still many cases of postoperative thrombosis and even embolism, in spite of whatever we do before or after operation. It appears to me that we have far from solved the problem, and much experimentation and clinical investigation are still needed, if we are to thoroughly understand and prevent this complication so far as it concerns the surgical patient.

Pulmonary embolism has been satisfactorily handled by immediate operation, but it requires a well-trained house staff and a sterile set-up for such an emergency. We have felt this to be a worthwhile routine, and the house staffs are each year given instruction in how to handle this emergency.



DOCTOR BREYER (Closing).—I appreciate the suggestions made by the discussers and the emphasis placed on certain phases of the subject, which I could not stress due to the shortness of the paper. The underlying surgical principle of the recommended exercises in the prevention of thrombosis is the effect of muscle action on the venous circulation. We all have made use of this principle, when we ask the donor for a blood transfusion, to open and shut his hand after the trochar needle has been inserted in the median basilic vein.

Dr. Alvin G. Foord, pathologist at our Huntington Memorial Hospital, has stated to me that when the autopsy surgeon of the pathologic service of Dr. Julius Erdheim of Vienna failed to find the source of the pulmonary embolism, Doctor Erdheim would ask if the veins of the calves of the legs had been dissected out and explored. Very often when this was done, the origin of the embolus was found to be there.

Exercises that will cause tensing of the flexors and extensors of the foot, and of the tensor femoris muscle, will produce the desired effect.

WHOOPIING COUGH: ITS PROPHYLAXIS AND TREATMENT*

By J. M. FRAWLEY, M.D.
Fresno

DISCUSSION by A. J. Scott, M. D., Los Angeles; Francis Scott Smyth, M. D., San Francisco; Charlotte Singer Brooks, M. D., San Francisco; Edward B. Shaw, M. D., San Francisco.

A PROGRAM directed toward the control of whooping cough has been carried on since 1932 in the public schools of Fresno. Two methods have been employed, viz., isolation and vaccination.

ISOLATION

In order to be of benefit as a factor in controlling the spread of whooping cough in the classroom, isolation has to begin at the onset of the cough. This is possible only when the cough-plate method¹ is used to detect early cases.

At the outset of this study, cough plates were made for us by Doctor Krueger at the bacteriological department of the University of California in Berkeley. They were always received in perfect condition, and the exposed plates were returned by mail after incubating overnight. During one school season they were sent to us by Doctor Kellogg from the State Department of Public Health Laboratories in Berkeley, but two years ago a cough-plate station was organized at the Fresno County Hospital, and the plates have been made and read there. They are prepared according to a method recommended by J. J. Miller.

TECHNIQUE

The technique is described in detail by Kendrick, Miller, and Lawson² in the American Public Health Association Year Book for 1935-1936:

A modification of Bordet and Gengou's potato blood agar is made as follows:

Base:

Peeled sliced potatoes, 500 mg.

Glycerin, U. S. P., 40 cc.

Distilled water, 1,000 cc.

Boil the potatoes in glycerin and water until soft. Make up to volume, strain through gauze and allow to stand for sedimentation. Siphon off the supernatant liquid.

To 500 cubic centimeters of clear potato extract add:

Sodium chlorid solution, 0.75 per cent, 1,500 cc.

Agar, Bacto, 60 gm.

Proteose Peptone, 20 gm.

Let stand for fifteen minutes, to saturate the agar. Heat until the agar is dissolved, and dispense in amounts convenient for storage. Autoclave for twenty-five minutes at fifteen pounds pressure (120 degrees centigrade). This base may be stored indefinitely.

Finished medium—To the melted base, at 45 degrees centigrade, add blood to make a final concentration of at least 15 per cent. The blood should be used when fresh, never more than seventy-two hours after it has been obtained. It may be from sheep, horse, or human source, but avoidance of horse blood for the vaccine medium is recommended. Mix the blood with the base by whirling, and pour into plates—about 15 cubic centimeters per Petri plate. Either glass plates or metal boxes may be used.

The potato extract-glycerin-agar base is kept stored in the ice-box, and sufficient Petri plates for a week's supply are made up by adding blood

* Read before the Pediatric Section of the California Medical Association at the sixty-fifth annual session, Coronado, May 25-28, 1936.

obtained from hypertension cases or from human placentas. The plates are kept in the ice-box until needed.

The detection of early cases rests with the school nurse. She must be on the lookout for suspects among the children, who are referred to her each morning by the teachers, and should take cough-plate cultures in all cases where there is any cough, especially in the case of children who are known to have been exposed to whooping cough.

The plate is uncovered and held five or six inches from the child's mouth. Gentle pressure over the trachea just below the larynx will elicit coughing, and after several good expulsive coughs the plate is covered and taken immediately to the incubator. In positive plates the characteristic tiny colorless hemispherical colonies appear, surrounded by a zone of hemolysis. The organisms are described as follows:²

Stained by Gram's method, *B. pertussis* decolorizes readily—much more readily, in fact, than does *H. influenzae*. Viewed microscopically, the small, faintly stained coccoid bacilli are scattered evenly throughout the film, occurring singly for the most part, seldom in chains of even two, and not found as pleomorphic threads. Frequently they show bipolar staining.

It takes forty-eight to seventy-two hours for the colonies to develop, and during that time a clinically suspicious case, or one with a history of exposure, must be treated as if positive. It is essential for the school nurse to have not only the coöperation of the teachers, but she must also have the good will of the practicing physician in the community. We have had splendid coöperation on the part of the physicians, and are occasionally called on to furnish cough plates to physicians for use in their private cases.

HOW STATE SUBSIDY FOR SCHOOL ATTENDANCE WORKS OUT

One of the chief obstacles to excluding children with incipient whooping cough lies in the system of granting state aid to schools, based on average daily attendance. Recently a school in Fresno County was closed down completely for a month. So many children were absent with whooping cough that the trustees decided it would be better to close the school than to allow the attendance to fall below a certain level. By keeping the school open with the decreased attendance they would have lost \$1,200 of next year's state grant.

This program of early isolation is not new. In Denmark, children are excluded from school during the early catarrhal stage, and allowed to return after the paroxysmal stage has been well established after the cough plates are consistently negative.

Besides the use of cough plates for diagnosis, a second measure which has been tried out in the Fresno public schools, has been prophylactic vaccination of kindergarten children. The opportunity is offered to each new class, and the vaccine given on the written request of the parent.

VACCINATION

The attitude toward vaccine as a prophylactic and therapeutic agent in whooping cough has

undergone a radical change within the past few years. The year 1931 seems to have been the turning point. In that year Leslie and Gardner³ published in the *Journal of Hygiene* their classical study on the phases of hemophilus pertussis. Previously, most of the vaccines used were entirely innocent of antigenic principle.⁴

However, in looking back over the earlier period, the work of Madsen⁵ and his coworkers at the Danish Serum Institute stands out as peculiarly in line with the later idea.

Greatly renewed interest in whooping cough research followed the appearance of Leslie and Gardner's work.

Sauer,⁶ in 1933, published his successful results of prophylactic vaccination using very large doses of unwashed Phase I organisms grown on human blood enriched by Bordet medium. He has taken the stand that vaccination is effective only when given as a preventive, and not as a curative measure. In his latest review⁷ of his own cases, published in the *American Journal of Public Health*, November, 1935, he says:

Bacillus pertussis vaccine, like typhoid vaccine, is an immunizing, not a curative, agent. A time interval of several months is required for immunization to be complete. About 10 per cent of the children injected with a total of 8 cubic centimeters of the approved commercial vaccine contracted pertussis when subsequently exposed to infection.

Doctor Park,⁸ at the meeting of the American Academy of Pediatrics in June, 1935, reported the result of an extensive investigation into the value of prophylactic vaccination carried out by the New York City Health Department with Mishulow's vaccine. This vaccine is made from Phase I organisms grown on sheep's blood agar, with one per cent of sheep-serum broth added on the surface of the medium after inoculation. Vaccines grown in this manner contain, in addition to the pertussis bacilli, a toxic substance which increases the stimulation of agglutinins. Doctor Park concluded that

The efficacy of pertussis prophylactic vaccination appears to depend primarily upon sufficient dosage.

A group of thirty-eight children were given seventy-seven to eighty-eight billion of the N. Y. C. Vaccine. Five of these were exposed to active cases, and none developed pertussis. Another group of 148 children were given thirty to seventy-five billion of the same vaccine; sixteen of them were exposed and nine developed pertussis, but four of these nine had no whoop, did not vomit, and the cough lasted only two or three weeks. They were so atypical that they could not have been diagnosed as cases of pertussis if they had not been definitely exposed. As the dosage decreased, the incidence became higher.

Kendrick and Eldering⁹ in January, 1936, reviewed the work on the prophylaxis of whooping cough being carried on by the Michigan Department of Health. Doctor Kendrick has used a vaccine which is a once-washed ten thousand million per cubic centimeter suspension of *B. pertussis*, Phase I of Leslie and Gardner, grown on Bordet-Gengou medium enriched with 15 per cent sheep's blood. The organisms are killed with merthiolate 1:10,000 or phenol 0.5 per cent allowed to act at cold-room temperature for a week or more.

A total dosage of 7 cubic centimeters is given, divided into four doses. Out of a large number of vaccinated children, follow-up work has indi-

TABLE 1.—Summary of Prophylactic Vaccination With Krueger's Pertussis U. B. A. (Commercial)

Dosage	Number of Children Vaccinated	Exposures	Developed Whooping Cough	Percentage of Failures
8.0 cc.	505	Home 30 School 68 Total 98	Mild 33 Moderate 6 Severe 4 Total 43	44.0%
12.0 cc.	113	Home 9 School 12 Total 21	Mild 6 Moderate 1 Severe 3 Total 10	47.6%

cated that of ninety-five who were subsequently exposed, thirteen (13.6 per cent) developed whooping cough. Of these, nine cases (9.2 per cent) were light or very light.

In an unvaccinated control group there were 128 exposures with 98 (88.2 per cent) cases of whooping cough. Of the ninety-eight cases, nineteen, or 19.3 per cent, were light or very light.

To review, briefly, the Michigan Department of Health reports that, after vaccination, 13.6 per cent of exposed children have developed whooping cough, while Sauer reports about 10 per cent of exposures among his vaccinated cases have developed whooping cough.

FRESNO PROCEDURE

In the vaccination program at Fresno, Krueger's Pertussis U. B. A.¹⁰ has been used. This vaccine* is a solution of endocellular antigen extracted from washed Phase I *H. pertussis* organisms by mechanical disruption and ultrafiltration.

By this method of preparation, including the thorough washing of the bacterial cells, the toxic filtrate which gives the reaction of Schwartzmann has been discarded with the washings. In a personal communication Doctor Krueger says that:

Bacterial filtrates have long been known to contain antigenic fractions and to be capable of inducing toxic reactions under certain conditions. It is also true that broth filtrates regularly contain nonspecific and irritating metabolites. I feel that one might well sacrifice some of the antigenic fraction present in the filtrate, in order to avoid nonspecific reactions. That the specific antigen resides in the cell itself is evidenced by the work of Miller, Browne, and McCrea,¹¹ who showed that the U. B. A. produces complement-fixing antibodies against *H. pertussis* when injected into rabbits. Similarly, complement-fixing antibodies were produced in children as well as agglutinins and precipitins in some instances, and by Miller and Browne,¹² who were successful in sensitizing guinea pigs with Phase I *H. pertussis* cultures, so that the classical Schultz-Dale reaction was obtained with pertussis U. B. A.

The first clinical reports¹³ published on pertussis undenatured bacterial antigen were promising. The antigen solution used was prepared in Doctor Krueger's laboratory, and the organisms used were recently isolated during a current epidemic and were grown on media enriched with human blood. The commercial product has been modified to some extent, in so far as sheep's blood is used in the culture medium.

This commercial product has been used in a sufficiently large number of cases to justify an evaluation at this time. It has been used as a prophylactic agent before exposure, in prophylaxis after exposure, and therapeutically after coughing has begun.

PROPHYLAXIS BEFORE EXPOSURE

During the last two school years Pertussis U. B. A.* was given as a prophylactic agent before exposure to two groups totaling 618 children. Some 505 children received 8 cubic centimeters, 113 received 12 cubic centimeters. Children in these groups who were subsequently exposed contracted whooping cough in a high percentage of cases, as shown in Table 1.

It must be concluded that in the dosage used, H. Pertussis U. B. A. failed to protect a sufficient percentage. However, as Doctor Park has pointed out, the efficacy of prophylactic vaccination depends primarily on sufficient dosage. The present commercial material contains only 10 milligrams of protein nitrogen per 100 cubic centimeters of antigen solution. It remains to be seen whether protection can be offered when adequate dosage is employed. In order to achieve this result, some means may have to be found of supplying the material in far greater protein nitrogen concentration.

PROPHYLAXIS AFTER EXPOSURE

The published reports on the use of Pertussis U. B. A. as a prophylactic agent after exposure have been summarized by J. J. Miller in a report on H. Pertussis U. B. A. (Krueger) given before the Laboratory Section of the American Public Health Association at Milwaukee, October, 1935. The vaccine he reported was used during the incubation period in ninety-eight cases; 50 per cent developed a cough which, in most cases, was mild or atypical.

This attack rate of 50 per cent of exposures compares favorably with an attack rate of 76.5 per cent of exposures in a group of unvaccinated children observed by Kendrick.¹¹

It would seem from the published reports that considerable benefit followed the administration of Pertussis U. B. A. during the period of incubation. The chief objection to its use lies in the large number of daily injections that are required.

THE USE OF PERTUSSIS U. B. A. IN TREATMENT

The use of vaccine in the treatment of whooping cough is based on the fact that the disease is one of prolonged duration, usually taking six to eight weeks for immunity to develop. In such a slowly progressing infection it is rational to attempt to hasten the development of immunity by artificial stimulation of antibody formation.

* The vaccine was furnished by the Eli Lilly Company.

TABLE 2.—Summary of Treatment With Krueger's Pertussis U. B. A. (Commercial)

Case Age	Treatment Began	Duration Treatment in Days	Dosage	Duration of Symptoms After Treatment Began
1 H. W. 2 years	Five days before onset of symptoms	7	57 cc.	Mild cough for one week.
2 B. K. 8 weeks	Three days before onset of symptoms	8	12 cc.	Severe coughing for one week.
3 B. B. 6 years	Two days before onset of symptoms	8	60 cc.	Mild atypical cough for eight days.
4 B. B. 13 months	Two days before onset of symptoms	13	85 cc.	Mild cough for two weeks. Whooped for three days.
5 S. H. 3 years	Coughing two days	10	27 cc.	Whooped very little for one week.
6 R. W. 2½ years	Coughing two days	6	60 cc.	Mild atypical cough for one week.
7 M. B. 3½ years	Coughing two days	4	20 cc.	Coughed for four days. Six days later took cold; whooped and vomited three days.
8 D. A. 17 months	Coughing two days	5	47 cc.	Mild cough for one week.
9 R. H. 18 months	Coughing two days	5	40 cc.	Cough lasted for three days. Whooped three times.
10 D. R. 2 years	Coughing three days	7	57 cc.	Coughed for one week.
11 C. S. 5 years	Coughing three days	7	33 cc.	Coughed for nine days. Whooped four days, vomited once.
12 B. A. 6 years	Coughing five days	6	48 cc.	Coughed for eight days. Whooped four days, vomited once.
13 C. A. 3½ years	Coughing five days	7	53 cc.	Coughed for eleven days. Whooped five days.
14 E. H. 2½ years	Coughing six days Whooping and vomiting one day	4	33 cc.	Coughed five days. Whooped and vomited three days.
15 B. P. 10 months	Coughing one week	5	10 cc.	Coughed four days.
16 T. F. 20 months	Coughing one week	9	43 cc.	Coughed ten days. Whooped and vomited three days.
17 L. H. 6 years	Coughing eight days	10	48 cc.	Coughed for twelve days. Whooped two days.
18 D. B. 3½ years	Coughing eight days Whooping two days	17	122 cc.	Coughed three weeks. Whooped and vomited severe eighteen days.
19 H. C. 2 months	Coughing ten days	9	14 cc.	Coughed for nine days.
20 A. J. 3 years	Coughing ten days Vomiting three days	11	40 cc.	Twelve days more of whooping and vomiting.
21 A. J. 7½ years	Coughing ten days Vomited once	6	23 cc.	Coughed for six days. Whooped two days.
22 M. H. 4½ years	Coughing ten days	7	53 cc.	Coughed for seven days. Whooped three days.
23 G. E. 8 years	Coughing eleven days	7	60 cc.	Coughed for seven days. Whooped two days.
24 G. E. 5 years	Coughing eleven days	7	60 cc.	Coughed for seven days.
25 P. L. 5 months	Coughing eleven days.	6	28 cc.	Coughed for five days. Two weeks later took cold, whooped and vomited three nights.
26 J. B. Adult	Coughing thirteen days.	5	36 cc.	Coughed for six days. Whooped and vomited for two days.
27 B. H. 1 year	Coughing thirteen days.	9	41 cc.	Coughed for thirteen days. Whooped five days, vomited one day.
28 R. Z. 3½ years	Coughing two weeks Whooping and vomiting four days	5	25 cc.	Coughed for six days. Whooped three days, vomited two days.
29 D. B. 10 months	Coughing two weeks Whooping and vomiting three days	9	68 cc.	Coughed for ten days. Whooped four days.
30 A. S. 3 years	Coughing two weeks	7	29 cc.	Coughed for nine days. Whooped five days, vomited four days.

(Continued on next page)

TABLE 2.—*Summary of Treatment With Krueger's U. B. A. (Commercial) (Continued)*

31 N. A. 3 years	Coughing two weeks Whooping and vomiting two days	11	78 cc.	Eleventh day of treatment stopped vaccine because of reaction. Whooping and vomiting for seventeen days.
Case Age	Treatment Began	Duration Treatment in Days	Dosage	Duration of Symptoms After Treatment Begun
32 S. P. 3 years	Coughing two weeks	5	14 cc.	Coughed for nine days.
33 F. G. 3½ years	Coughing two weeks Whooping and vomiting two days	5	19 cc.	Coughed one week. Whooped and vomited three days.
34 J. C. 6 years	Whooping and vomiting for two weeks	18	54 cc.	Coughed for three weeks. Whooped and vomited fourteen days.
35 J. W. 5 years	Coughing eighteen days Whooping ten days	8	80 cc.	Coughed for nine days. Whooped for seven days.
36 P. Mc. 18 months	Coughing eighteen days Severe whooping and vomiting three days	9	43 cc.	Coughed for ten days Whooped and vomited six days.
37 D. Mc. 4 years	Coughing three weeks Severe whooping and vomiting	10	68 cc.	Coughed, whooped and vomited for ten days more.
38 B. W. 2 years	Coughing three weeks Severe whooping and vomiting one week	5	25 cc.	Coughed for six days. Whooped and vomited three days.
39 T. P. 5 years	Severe coughing six weeks, whooping and vomiting two weeks	5	23 cc.	Stopped whooping and vomiting in five days.

The logical agent to bring about this objective would be a lysed vaccine. In such a vaccine there is a minimum of alteration of the antigenic properties, and the antibody stimulation begins at once without any preliminary period being required for the liberation of the antigen by bacteriolysis. Krueger's pertussis antigen is a vaccine of this type and, theoretically, meets all requirements. In practical use it has received considerable favorable attention.

To a recent questionnaire, replies were received from 162 pediatricians who had used Pertussis U. B. A. in the treatment of over 3,700 cases of whooping cough, and 104 (63 per cent) reported favorably.

However, in these cases no controls were used; and in a disease so variable in duration and severity as whooping cough, adequate controls, while difficult to obtain, are necessary.

Recently, I have had the opportunity to use the antigen in treatment in a small series of approximately forty cases, using as controls an equal number of cases observed simultaneously in the same schoolrooms, although obviously not from the same families. Large doses were given subcutaneously, 5 cubic centimeters daily or twice daily to children over one year of age, 2 to 5 cubic centimeters to children less than one year. Daily records were kept in both series on the number of coughing spells each night, the number of vomiting attacks, etc.

CONCLUSIONS

While this series is too small to form the basis of any definite conclusions, nevertheless it would seem that, in some cases at least, a modifying influence was exerted. The average duration of coughing for all children receiving daily vaccine injections was 2.7 weeks, with an average parox-

ysmal stage of 1.2 weeks. In the control group, the average duration of coughing was 6.5 weeks, with whooping and vomiting for 2.7 weeks.

The best results were obtained when injections were begun either during the incubation period or on the first day or two of coughing, or else in the late stages after the disease had passed its peak. There was no certainty about the influence which could be expected when injections were begun during the height of the infection.

SUMMARY

1. Krueger's Pertussis undenatured bacterial antigen (commercial) was used as a prophylactic agent in two groups of children, totaling 618. Protection against whooping cough was found to be insufficient to justify its use in prophylaxis before exposure.

2. In prophylaxis after exposure, and in treatment of early cases of whooping cough, modification of the expected course of the infection followed the administration of large daily doses of antigen. The average duration of coughing in thirty-nine children given injections was 2.7 weeks, with a paroxysmal stage of 1.2 weeks; in an equal number of controls the average duration of coughing was 6.5 weeks, with a paroxysmal stage of 2.7 weeks.

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DISCUSSION

A. J. Scott, M.D. (1401 South Hope Street, Los Angeles).—The use of the Krueger U. B. A. pertussis for prophylaxis is still too new to permit the passing of a positive judgment upon it. This preparation for treatment is apparently not satisfactory because of the large doses, the high cost, and the frequency of doses.

The cough plate method of diagnosis is the most satisfactory, but the technical difficulties of preparation and plate distribution must be overcome before it can be used universally in our private or clinic practice.

Our experience with U. B. A. pertussis is very limited. In the few cases where we have used it for prophylaxis, we have not had any pertussis. We have used it for only two years, and this is too short a time to prove anything. In treatment we have been disappointed, probably because we did not use the large doses Doctor Frawley has used.

In an experience of ten years, from 1925 to 1935, we took 155 cases of pertussis from our personal files. These had no prophylaxis and were diagnosed by blood counts and clinically. We treated them with a stock pertussis vaccine of 7,500 million per cubic centimeter, giving one-half to one and one-half cubic centimeters every other day for three doses. In addition, we used quartz lights and, occasionally, codein. The average amount of vaccine used in 128 cases was 3.78 cubic centimeters per child. The average number of weeks of coughing was 2.36, and the average number of visits was 6.89.

In the California Babies' Hospital, for the same period, we had 2,569 cases. There we averaged 1.75 cubic centimeters of vaccine per child, and the mothers reported improvement in 70 per cent of cases.

We appreciate that pertussis is a variable disease, some years being more severe than in others; also, unless controls are used, as Doctor Frawley says, we can really prove very little. However, we feel that we have had as good results with big doses of stock concentrated pertussis vaccine as have been reported with the more expensive U. B. A. pertussis.

Theoretically, the U. B. A. pertussis is the proper vaccine to use if we are going to use a vaccine. But time and experience will prove whether it is as valuable as the stock H. pertussis vaccine, Phase 1, of our reliable biological laboratories. I hope Doctor Frawley is encouraged enough to continue this work, and to report again what progress he is making.

FRANCIS SCOTT SMYTH, M.D. (University of California Hospital, San Francisco).—The Pediatric Department of the University of California has been intensely interested

in the study of whooping cough. We have learned that it is a more variable disease in its symptomatology than was previously stressed, and were it not for the cough plate many cases, both in adults and children, would go unrecognized. The variability in individual susceptibility, as well as the variation in virulence of the organism, complicate the statistical study of the disease and its prophylaxis. Dr. John J. Miller, Jr., and Dr. Charlotte Singer Brooks have very carefully observed their group of children with sibling control. This method is, of course, more accurate than control cases selected at random. While our earlier studies with U. B. A. were more encouraging, we are not so impressed with the results in this intimate group.

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CHARLOTTE SINGER BROOKS, M.D. (University of California Hospital, San Francisco).—Doctor Frawley's effort to control whooping cough among school children by the use of the cough plate is very commendable. From the viewpoint of practical epidemiology, the cough plate finds its greatest utility in detecting the early case of whooping cough.

We have been using both U. B. A. and Phase 1 pertussis vaccine in a well-controlled group of children in our pertussis immunization study in San Francisco. The status of Phase 1 H. pertussis vaccine in this group is still an open question. We have not had sufficient exposures among these children to be able to draw conclusions at this time. The incidence of pertussis in our U. B. A. immunized children and control children who have been adequately exposed to the disease has been 100 per cent. The cases of pertussis were of all grades of severity. I believe the criteria of adequate exposure need to be stressed before concluding that immunization is efficacious. Indirect exposure to an early case, or direct exposure to a child late in the paroxysmal stage, may not mean exposure to living H. pertussis bacilli. It is well known that positive cough plates are obtained with difficulty, and often not at all late in the disease. Not until definite standards or criteria of exposure are used, and the status of natural immunity is determined, can conclusions be drawn as to protection of immunized children.

I regret that our experience with U. B. A. in treatment of pertussis cases, well controlled, has been most discouraging. We are not able to confirm Doctor Frawley's splendid results, nor those of Stallings and Nichols, with this agent. The disease in our treated cases was of practically the same duration and severity as in our control cases, regardless of the stage of the disease at which the treatment was instituted. Details of our experience with the therapeutic value of U. B. A. in the treatment of pertussis are to be published shortly.

It is well known that commercial U. B. A. endo-antigen contains very small amounts of protein nitrogen and that there is a variation of the amount in each lot. The lyophil process might serve to concentrate this antigen and standardize its nitrogen content. A study of the therapeutic value of a standardized concentrated U. B. A. antigen would be of scientific interest. However, the results of our experience with the present expensive commercial product make it doubtful whether the additional expense of such concentration and standardization is warranted.

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EDWARD B. SHAW, M.D. (384 Post Street, San Francisco).—Doctor Frawley has detailed a method for the early recognition and subsequent isolation of whooping cough cases which is perfectly feasible, but which can be accomplished only by means of painstaking care and close cooperation between school authorities, parents, children, school nurses, and physicians. The severity of the disease entirely justifies the labor involved. It should be pointed out, however, that although whooping cough is hardly more than an annoying problem among school children, it is a much more serious one in the home among children below school age, especially infants, and methods of control in the home are of far greater importance than those for the schoolroom.

When one member of a family develops recognizable whooping cough, other members of the family have almost inevitably been exposed and will usually develop the dis-

ease in the absence of immunity. Parents and physicians frequently lose sight of the fact that it is worth while to endeavor in every way to diminish the *intimacy of exposure* of well children to those affected with the disease. Cases which develop from intimate exposure (secondary cases in the family) are commonly more severe than is the original. Even though absolute isolation cannot be maintained in the home, every effort should be made at segregation of the ill child, thus reducing the exposure dosage to which other members of the family, frequently smaller children, are subjected.

I am in agreement with the moderation of the author's viewpoint concerning prophylactic and therapeutic use of vaccine. The prophylactic use of vaccine seems commonly to have been accepted with an enthusiasm scarcely justified by the available data. There is no question as to the extreme desirability of a method for immunization, and there seems to be little reason to fear dangerous effects of the vaccine, although the repeated injection of large amounts of the preparation is somewhat of an unpleasant ordeal for little children. The degree and duration of the protection so conferred is, however, most difficult of precise evaluation. There is no simple test for immunity. There is no evidence to suggest that the immunity will be enhanced and maintained by a natural method of immunization. The duration and effectiveness of immunity can be determined only by prolonged observation of the response to natural exposure among large groups of vaccinated and unvaccinated children. There are many variable factors which are most difficult to control. The accumulation of adequate data will not quickly be accomplished, and the widespread employment of active immunization, except on an experimental basis, should be deferred until the questions involved can be answered with authority.

PRACTICAL QUANTITATIVE PERIMETRY*

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DISCUSSION by George L. Kilgore, M.D., San Diego; Clifford B. Walker, M.D., Los Angeles; Joseph William Crawford, M.D., San Francisco.

THERE have been many definitions of the field of vision. Some of them are very ingenious in their method of clarifying a difficult subject, but many of them, although technically correct, are clinically worthless.

By far the most lucid and understandable of these definitions, and the one which best explains and illustrates the problems of modern quantitative perimetry, is that of Traquair.¹ In this definition, the field is imagined as an island of vision surrounded by a sea of blindness.

The island is oval in shape and the coast line rises steeply, as cliffs, vertical on one side and sharply sloping on the other. Above the cliffs is a sloping plateau which rises more rapidly again toward the somewhat eccentrically situated and sharp summit. To one side of this point is a pit (the blind spot) extending down to the level of the surrounding sea.

To an observer situated in the air, above the pinnacle of the summit, a panoramic view of the whole island is presented. Now, conceive of the surface of such a hill as not stationary but subject to slight fluctuations in height, distortion or partial destruction with depressions of every variety occurring on its surface, of all sizes, shapes

and depths, and we have a picture of the normal and pathologic field of vision.

CHARTED PERIMETRIC FIELD A CONTOUR MAP

Modern quantitative perimetry is a true *survey* of this hill with all its different levels, dips, and depressions shown by contour lines. Thus, the perimetric field, as charted, is a contour map. It is no longer sufficient merely to outline the coast of this island or very deep depressions in its surface. On the contrary, it is the shallow, barely perceptible indentations which give us the earliest and most valuable information.

In spite of the seemingly complicated nature of this type of examination of the field of vision, it requires in reality only the utilization of a few simple principles and the simplest and most inexpensive equipment. It is, therefore, eminently practical and of the greatest value for routine use in the office of the busy practitioner.

PERIMETRY METHODS

Surprising as it may seem, almost half a century was allowed to elapse after Bjerrum² discovered the value of his consulting-room door as a perimeter, before even a limited enthusiasm was aroused by his method. This apathy has persisted in spite of the early recognition of his work by Sinclair³ and its more full development by Ronne,⁴ Walker,⁵ and Traquair. It is safe to say that at the present time there are many ophthalmologists, neurologists, neurosurgeons, and others, to whom the accurate charting of the field of vision is of the greatest value, who are not fully cognizant of quantitative perimetry and its possibilities. Of those who use it properly and to its full advantage, there are probably only a handful.

Any attempt to introduce or advocate a method of examination which is cumbersome and lengthy, no matter how excellent theoretically, is bound to end in failure if it has not a highly practical aspect which will recommend it to many men for their routine use.

It was Clifford Walker who showed that quantitative perimetry *could* be a practical method of examination. In doing so, he has gone into the mathematics of tangents, visual angles, distances, time, etc., all of which have been necessary and of great value in the development of the science of perimetry. The complexity of the subject, however, has frightened many men into neglecting it, and yet it is upon this complicated foundation that the present-day clinical methods of field-taking and interpretation are built.

When we speak of practical quantitative perimetry, we must necessarily confine ourselves to a working method which is applicable to all types of cases and which can be used in routine office practice. Walker and Traquair have shown us the way by developing a practical clinical method of perimetry. It behooves all of us to take full advantage of their methods of examination.

For a study of the visual fields, two types of examination are necessary. The perimeter is used to obtain information of the peripheral field and the field for large visual angles, while the more

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